REMARKS

Support for new Claim 36 can be found in original Claims 10-14 and on page 6, lines 3-15 of the present specification.

In paragraph 2, on page 2 of the Office Action, the Examiner contends that the specification fails to meet the sequence listing requirements because there are sequences, for example, at page 9, which do not contain a sequence identifier.

Accordingly, Applicants submit simultaneously herewith an appropriate Sequence Listing and amend the specification to include the sequence identifiers as requested by the Examiner.

In paragraph 3, on page 2 of the Office Action, the Examiner objects to the specification because it does not contain an Abstract.

Applicants hereby add an Abstract to the present specification, as requested by the Examiner. The Examiner is requested to note that the added Abstract corresponds to the Abstract of the parent PCT application.

In paragraph 4, on page 3 of the Office Action, the Examiner objects to the specification because it does not contain a separate section entitled "Brief Description of the Drawings". The Examiner notes that this objection can be overcome by amending page 10 [*sic* page 11] of the present specification, to insert "Brief Description of the Drawings".

Applicants hereby amend the specification as requested by the Examiner.

In paragraph 6, on page 3 of the Office Action, the Examiner rejects Claims 15-32 under 35 U.S.C. § 112, first paragraph.

Specifically, the Examiner states that the specification is enabling for the following methods:

(1) where the genotype FcγRIIA H/H, FcγRIIIB NA1/NA1 or a combination thereof in a human afflicted with multiple sclerosis is indicative of a benign prognosis;

(2) where the genotype FcγRIIA R/R, FcγRIIIB NA2/NA2 or a combination thereof in a human afflicted with myasthenia gravis is indicative of a benign prognosis;

(3) where the genotype FcγRIIIB NA1/NA1 in a human afflicted with myasthenia gravis is indicative of a non-benign prognosis; and

(4) where the genotype FcγRIIA H/H, FcγRIIIB NA1/NA1 or a combination thereof in a human afflicted with diabetes mellitus is indicative of a non-benign prognosis.

However, the Examiner contends that the specification is not enabling for the following methods:

(1) methods involving non-human subjects,

(2) where the genotype FcγRIIIB NA2/NA2 in a patient suffering from cerebrovascular disease, cardiovascular disease or atherosclerosis is indicative of a non-benign prognosis,

(3) where the genotype FcγRIIA H/H in a patient afflicted with Addison's disease is indicative of a non-benign prognosis, or

(4) where any Fc receptor genotype, including any Fcγ receptor genotype, is detected in order to determine the

prognosis for any of the diseases and conditions recited in Claims 15 and 30, other than the specific examples recited above (i.e., those of Claims 18-20 in human subjects).

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

With regard to the Examiner's objection that the specification is not enabled for non-human mammals, solely in order to advance the prosecution, Applicants have amended the claims to specify that the mammalian subject is a human subject.

Furthermore, Applicants respectfully disagree with the Examiner's assertion that Claim 21 (directed to the prognosis of each of cerebrovascular disease, cardiovascular disease and atherosclerosis) is not enabled by the present specification. Indeed, there is sufficient information in the specification to allow the prognosis of each of cerebrovascular disease, cardiovascular disease and atherosclerosis in accordance with the present invention. Claim 21 itself clearly indicates that the genotype Fc RIIIB NA2/NA2 is associated with a non-benign prognosis of each of these diseases, and thus the information content of the claim itself, when read in conjunction with the specification, provides enough information to enable these prognostic methods to be carried out without an undue burden.

Moreover, the data shown in Example 4 of the specification provides evidence that the NA2/NA2 genotype is associated with the non-benign prognosis of atherosclerosis. In this regard, the Examiner is requested to note that the column headed "NA2/NA2" in Table 4 shows that the NA2/NA2 genotype is found in 52.4% of patients with atherosclerosis, but is only found in

approximately 40% of healthy patients or non-atherosclerotic patients.

Additionally, the Examiner is requested to note that Example 6 provides enablement for Addison's disease. On November 19, 2002, the undersigned contacted the Examiner and brought Example 6 to the Examiner's attention. The Examiner advised that she has agreed to withdraw the rejection regarding Addison's disease, i.e., she now considers item (3) (Claim 22) is enabled by the specification (see Interview Summary Record dated November 19, 2002).

With regard to the Examiner's objection that the claims relating to the detection of any Fc receptor genotype are not enabled, solely order to advance the prosecution, Applicants have amended the claims to specifying that the Fc receptor is an Fcγ receptor (i.e., to limit the claims to incorporate the feature of Claim 16, which is hereby cancelled).

The present invention is based on the finding that variants of Fcγ receptors are associated with the specific diseases as set out in Claim 15 and that, once this has been ascertained, it is straightforward (i.e., would involve no undue experimentation) for the skilled person, based on the teaching of the specification, to compare the genotypes of Fcγ receptors from normal subjects and diseased subjects in accordance with the method of Claim 15 in order to determine whether a non-benign or benign prognosis should be given for the specified diseases. In this regard, the Examiner is requested to note the steps in Claim 15, and also the specification on page 8, lines 4-22, describe that it is straightforward to determine the benign or

non-benign genotypes for particular Fcγ receptors for the selected diseases.

According, Applicants respectfully submit that the claims are enabled by the present specification, and thus request withdrawal of the Examiner's rejection.

In paragraph 8, on page 6 of the Office Action, the Examiner rejects Claims 15-32 under 35 U.S.C. § 112, second paragraph.

Specifically, with respect to Claims 15-29 and 32, the Examiner states that the claims are indefinite in the recitation "determining, as a genetic marker".

In view of the amendment to Claim 15 to delete therefrom the redundant expression "as a genetic marker", Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot.

With respect to Claims 15-32, the Examiner states that these claims are unclear as to how the Fc receptor obtained from a "normal mammalian subject" or a "diseased mammalian subject" in step (b) and (c) of Claims 15 and 30, respectively, relates to the "at least one Fc receptor" in step (a).

In view of the amendment to step (b) of Claim 15, and step (c) of Claim 30 to recite "a corresponding Fcγ receptor", Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot.

With respect to Claims 16-17, the Examiner contends that these claims are indefinite in referring to "said Fc receptor", i.e., the Examiner asks whether this recitation is intended to refer back to the "at least one Fc receptor" of Claim 15 or to

the Fc receptor from the normal or diseased subject or to each of these.

The Examiner is requested to note the Fc receptor in Claim 16 is intended to refer to the "at least one" Fc receptor and the "corresponding" Fc receptors. In any event, in view of the cancellation of Claim 16, Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot.

With respect to Claims 23, 27-29 and 31, the Examiner contends that these claims are indefinite because it is unclear how these claims further limit Claims 15 and 30 in the instance where the "genotype...from a normal mammalian subject" is employed.

In view of the amendments to Claim 23 to refer to the situation "when a non-benign prognosis is made", Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot.

With respect to Claims 30-31, the Examiner contends that these claims are indefinite because it is unclear as to what diagnosis would result where the genotype of a normal mammalian subject is employed.

In view of the amendments to Claim 30 to recite"...comparing the thus determined genotype of DNA encoding an Fc receptor obtained from a normal mammalian subject and to the genotype of DNA encoding an Fc receptor obtained from a diseased mammalian subject...", Applicants respectfully submit that this aspect of the Examiner's rejection has been rendered moot.

In paragraph 10, on page 8 of the Office Action, the Examiner rejects Claims 15-17, 23, 26-27 and 30-32 under 35 U.S.C. § 102(b) as being anticipated by Kimberly et al. Specifically, the Examiner contends that Wegener's granulomatosis (WG) taught in Kimberly et al is a type of cardiovascular disease.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

Applicants disagree with the Examiner's assertion that WG is a type of cardiovascular disease. Contrary to the Examiner's contention, there is no explicit teaching in Kimberly et al that WG is a type of cardiovascular disease (it is merely indicated that WG is a type of systemic vasculitides - see page 6, line 13). According to "Harrison's principles of internal medicine, 14th edition" (which is one of the major textbooks in internal medicine), "WG is a distinct clinicopathological entity characterized by granulomatous vasculitis of the upper and lower respiratory tracts together with glomerulonephritis. In addition, variable degrees of disseminated vasculitis involving both small arteries, and veins may occur". Small vessels do not include major cardiac or neck/brain vessels, i.e., cardiovascular disease is not part of this "small-vessel vasculitis". Thus, Applicants respectfully submit that WG is clearly not a cardiovascular disease.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested in Kimberly et al, and thus request withdrawal of the Examiner's rejection.

In paragraph 13, on page 9 of the Office Action, the Examiner rejects Claims 25 and 29 under 35 U.S.C. § 103 as being unpatentable over Kimberly et al in view of Herridge et al.

Specifically, the Examiner states that while Kimberly et al does not disclose surgical intervention as the treatment for Wegener's granulomatosis, Herridge et al teaches surgery as a form of treatment for some symptoms of Wegener's granulomatosis. Hence, the Examiner concludes that, in view of the teachings of Herridge et al, it would have been obvious to modify the method of Kimberly et al to include the further step of surgical intervention following determination of a non-benign prognosis in cases of Wegener's granulomatosis.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

As discussed above, Claim 15 from which Claims 25 and 29 directly or indirectly depend, is not taught or suggested in Kimberly et al, and it is clear that Herridge et al does not provide the deficiencies which exists therein.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested in Kimberly et al alone or when combined with the teachings of Herridge et al, and thus request withdrawal of the Examiner's rejection.

In paragraph 14, on page 10 of the Office Action, the Examiner rejects Claim 21 under 35 U.S.C. § 103 as being unpatentable over Kimberly et al in view of Bux et al.

Specifically, the Examiner states that Bux et al discloses that the NA2/NA2 genotype is associated with neutropenia in some individuals, and that neutropenia may trigger cerebral

hemorrhage, a type of cerebrovascular disease. Hence, the Examiner concludes that in view of Bux et al, it would have been obvious to modify the method of Kimberly et al so as to detect the presence of the NA2/NA2 genotype in a neonate as an indicator of a "non-benign" prognosis of increased risk for neonatal neutropenia as compared to a neonate with, e.g., a NA-null genotype.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

Although Bux et al may disclose that the NA2/NA2 genotype is associated with neutropenia in some individuals, Applicants respectfully submit that Bux et al can not be interpreted to indicate that a causal link or an increased risk is demonstrated between neutropenia and cerebral haemorrhage. In this regard, only one in four of the cases reported in Bux et al (case report No. 2 in column 2 on page 1027) suffered a cerebral haemorrhage. Applicants respectfully submit that this cerebral haemorrhage could have been caused by any number of factors other than neutropenia. In particular, it should be noted that the neonate which suffered the cerebral haemorrhage was quite premature and that any one of many complications arising from this premature birth, for example the severe respiratory distress which was suffered by this neonate, are likely to have caused or given rise to the increased risk of the cerebral haemorrhage. Thus, Applicants submit that the cerebral haemorrhage observed in case report No. 2 is no more than coincidence with the NA2/NA2 genotype.

Hence, there is no evidence from Bux et al that neutropenia positively triggers or results in an increased risk of cerebral haemorrhage, and hence there is no reason that a skilled person would have combined the teaching of Kimberly et al and Bux et al, and decide that the NA2/NA2 genotype could be used to prognose cerebral haemorrhage.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested in Kimberly et al alone or when combined with the teachings of Bux et al, and thus request withdrawal of the Examiner's rejection.

In paragraph 15, on page 11 of the Office Action, the Examiner rejects Claims 24 and 28 under 35 U.S.C. § 103 as being unpatentable over Kimberly et al in view of Bux et al, and in further view of Van Nostrand et al.

Specifically, the Examiner states that while Kimberly et al and Bux et al do not teach subjecting the test subject to diagnostic imaging, Van Nostrand et al discloses that a cerebral hemorrhage is diagnosed by an imaging method. Hence, the Examiner concludes that it would have been obvious to modify the method of Kimberly et al in view of Bux et al to include an additional step of diagnostic imaging.

For the following reasons, Applicants respectfully traverse the Examiner's rejection

As discussed above, Claim 15 from which Claims 24 and 28 directly or indirectly depend, is not taught or suggested in Kimberly et al in view of Bux et al, and Van Nostrand et al does not provide the deficiencies which exists therein.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested in Kimberly et al alone or when combined with the teachings of Bux et al and Van Nostrand et al, and thus request withdrawal of the Examiner's rejection.

In view of the amendments to the specification and claims, the submission of an Abstract herewith and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,

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